8 SHEETS DRWS

Figure 1

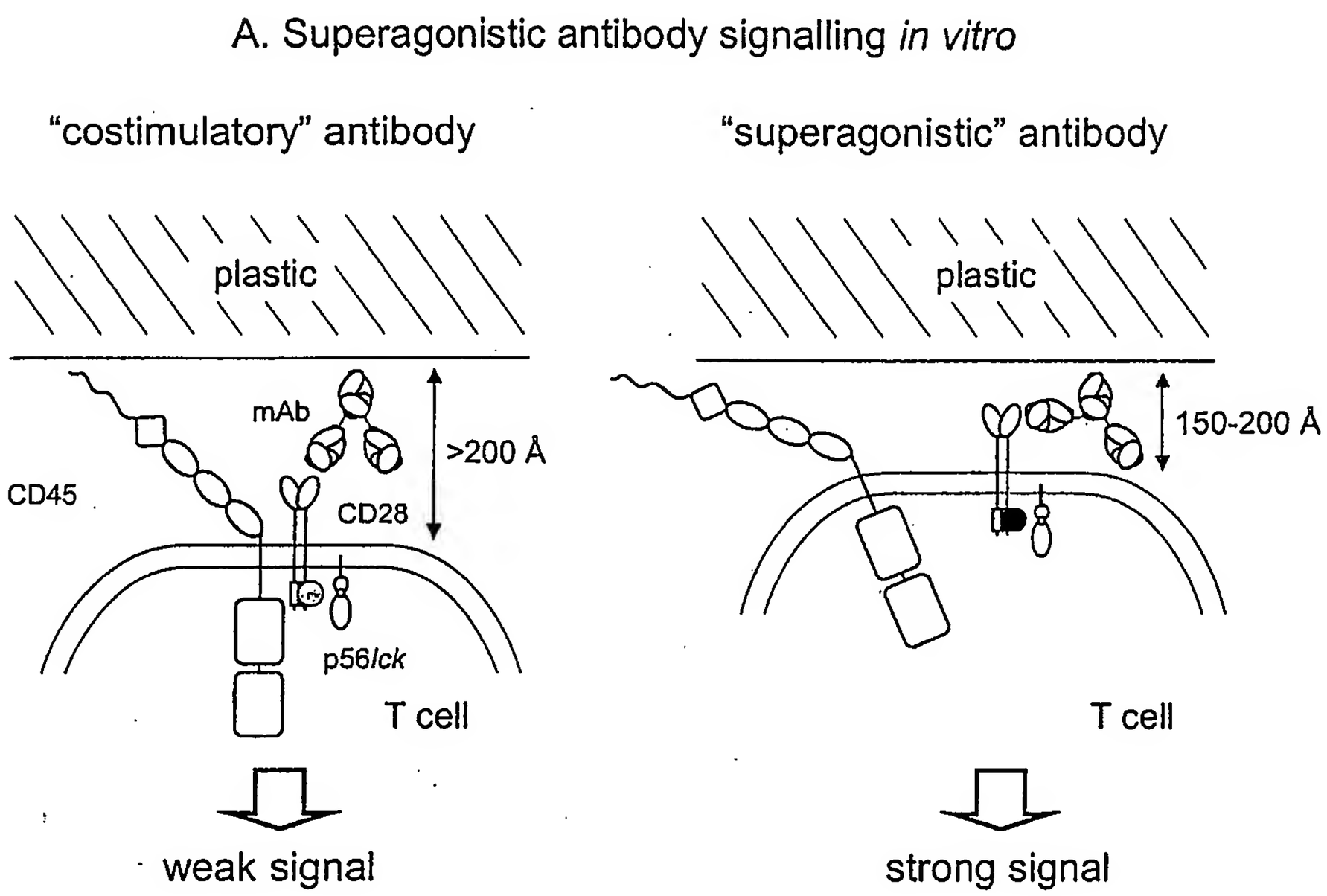

Figure 1

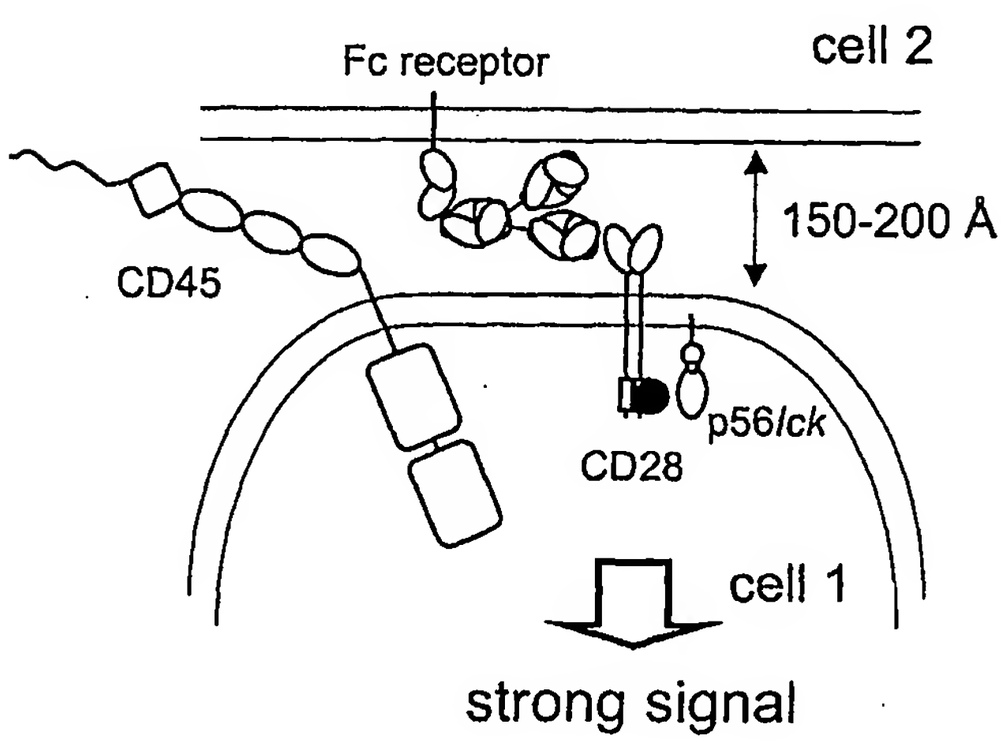
B. Superagonistic antibody signalling *in vivo*
Fc receptor
cell 2
150-200 Å
CD45
p56*lck*
CD28
cell 1
strong signal

Figure 1

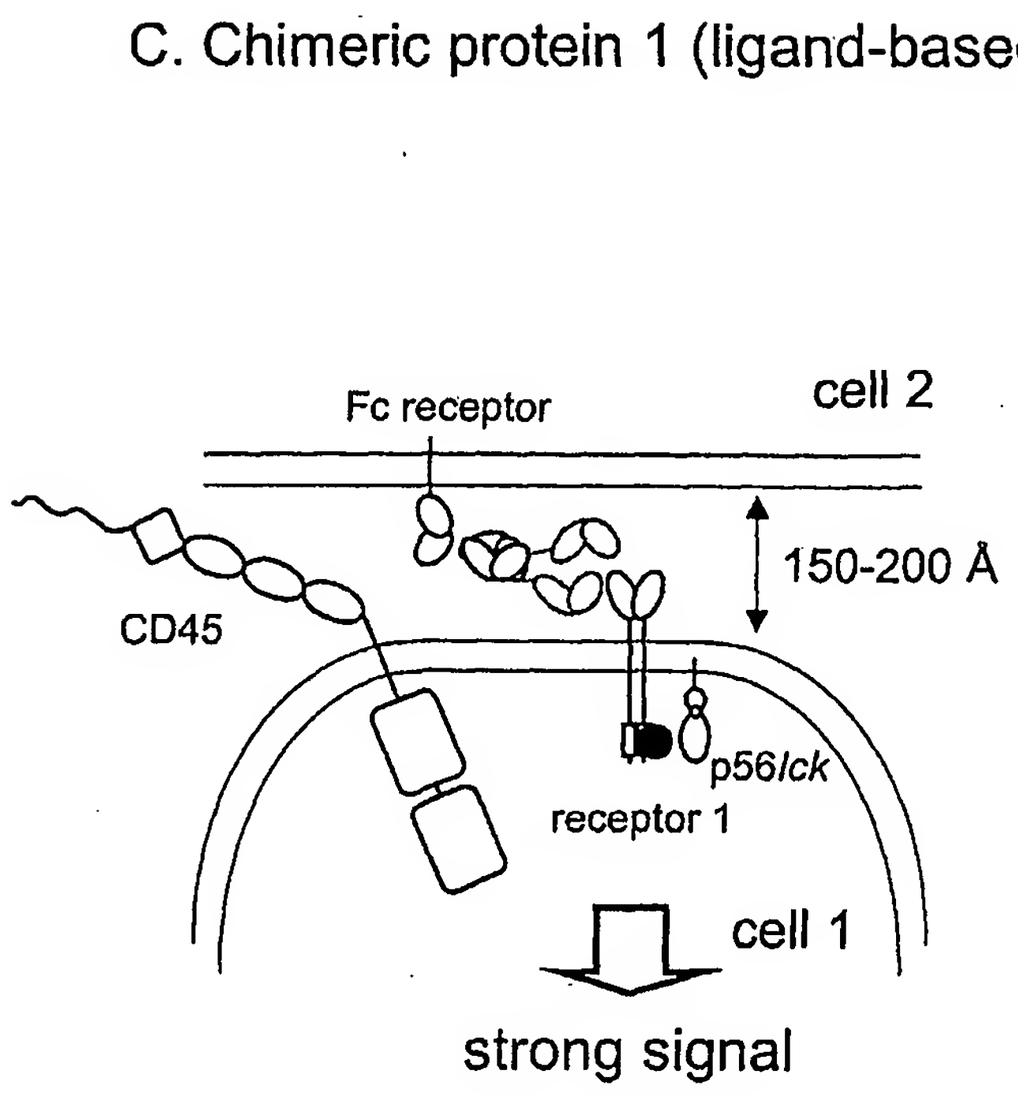
C. Chimeric protein 1 (ligand-based)
Fc receptor
cell 2
150-200 Å
CD45
p56lck
receptor 1
cell 1
strong signal
chimeric ligand/Fc superagonist:
• binds Fc receptor on cell 1
and receptor 2 on cell 2

Figure 1

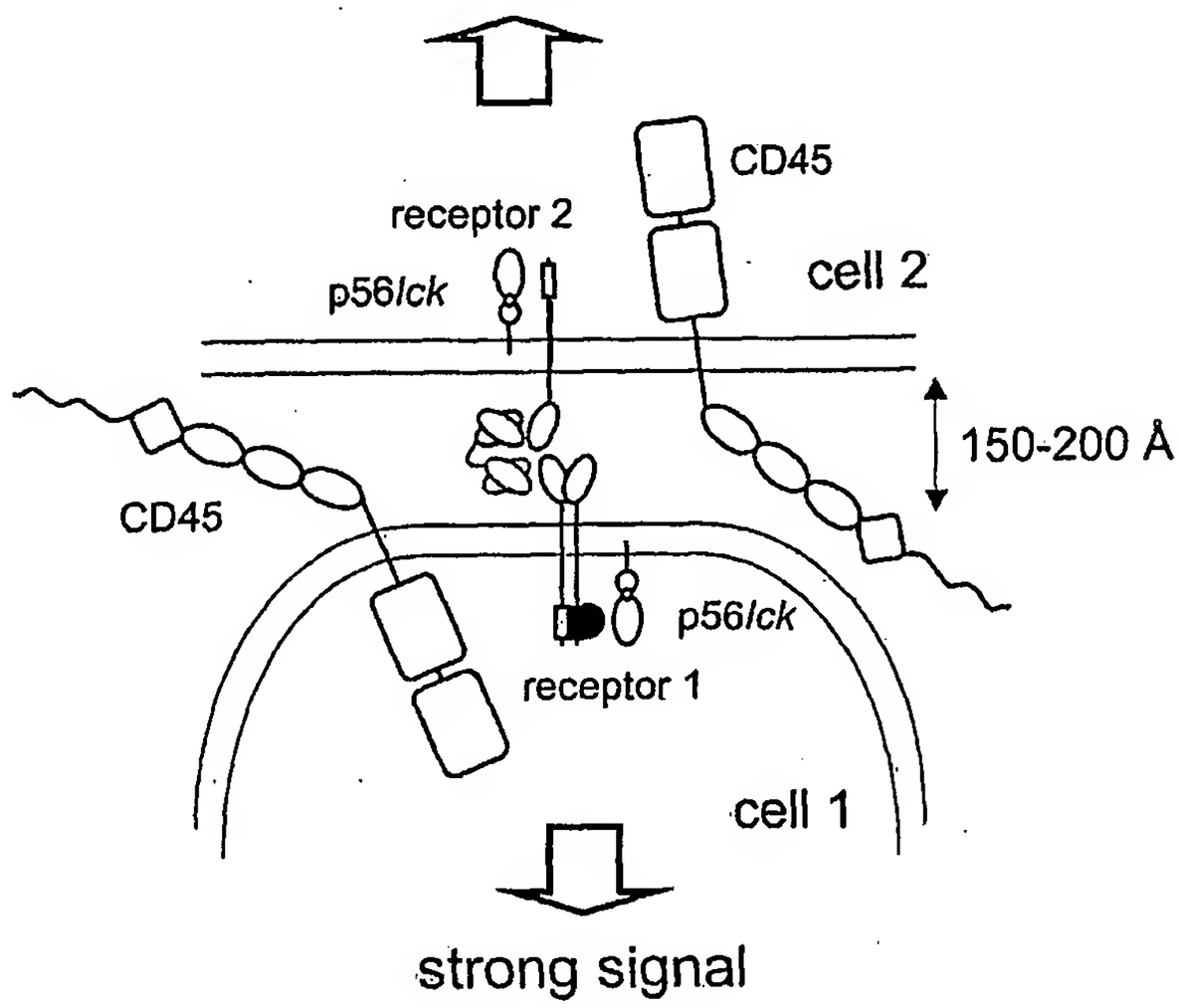
D. Chimeric protein 2 (Fv-based)
strong signal
CD45
receptor 2
p56lck
cell 2
150-200 Å
CD45
p56lck
receptor 1
cell 1
strong signal
chimeric Fv superagonist:
• binds receptor 1 on cell 1
and receptor 2 on cell 2

Figure 2

A

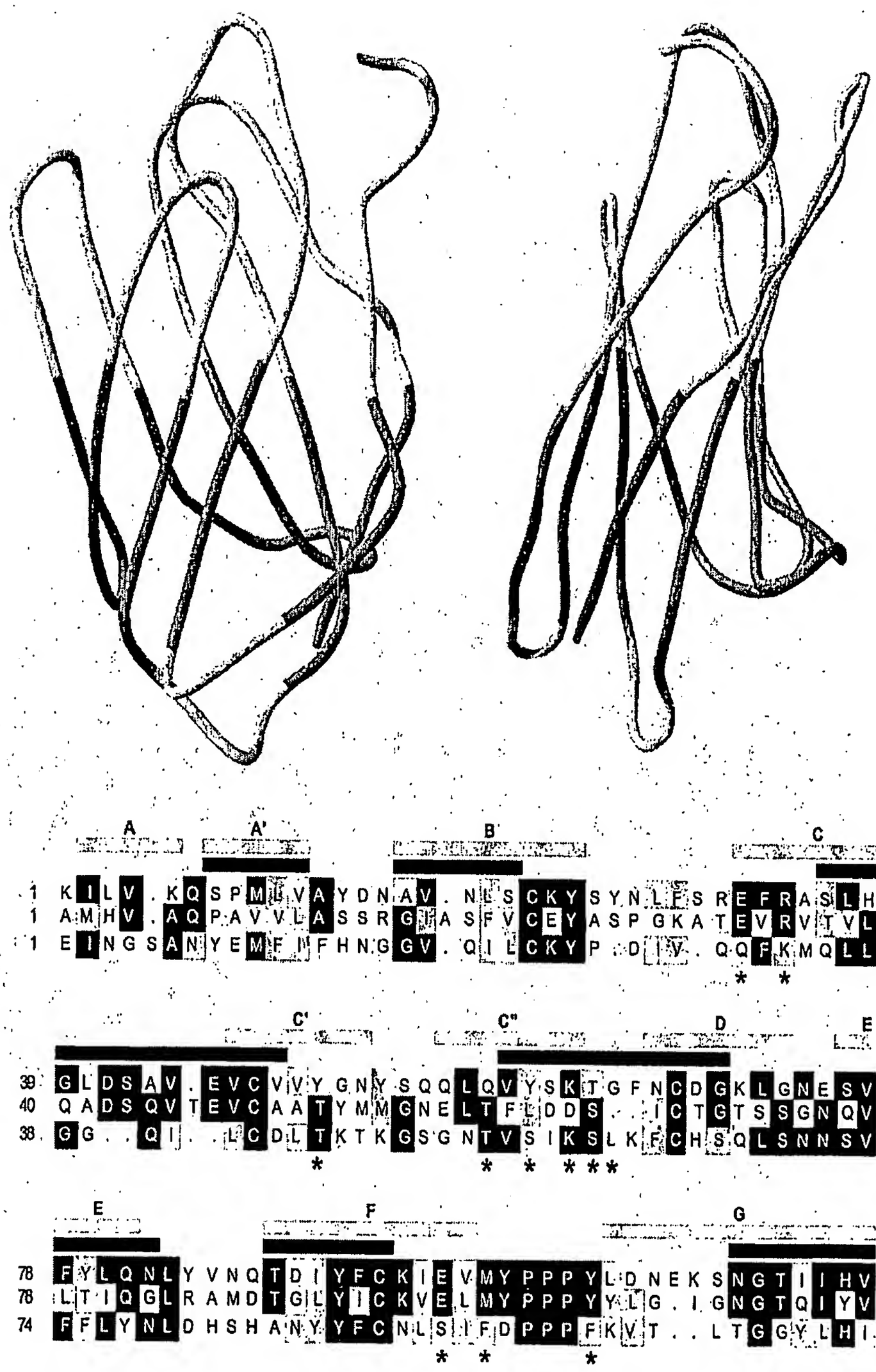
A
A'
B
C
hCD28 1 K I L V . K Q S P M L V A Y D N A V . N L S C K Y S Y N L F S R E F R A S L H K 38
hCTLA-4 1 A M H V . A Q P A V V L A S S R G I A S F V C E Y A S P G K A T E V R V T V L R 39
hICOS 1 E I N G S A N Y E M F I F H N G G V . Q I L C K Y P D I V . Q Q F K M Q L L K 37
C'
C"
D
E
hCD28 39 G L D S A V . E V C V V Y G N Y S Q Q L Q V Y S K T G F N C D G K L G N E S V T 77
hCTLA-4 40 Q A D S Q V T E V C A A T Y M M G N E L T F L D D S . . I C T G T S S G N Q V N 77
hICOS 38 G G . . Q I . . L C D L T K T K G S G N T V S I K S L K F C H S Q L S N N S V S 73
E
F
G
hCD28 78 F Y L Q N L Y V N Q T D I Y F C K I E V M Y P P P Y L D N E K S N G T I I H V 116
hCTLA-4 78 L T I Q G L R A M D T G L Y I C K V E L M Y P P P Y Y L G . I G N G T Q I Y V 115
hICOS 74 F F L Y N L D H S H A N Y Y F C N L S I F D P P P F K V T . . L T G G Y L H I 110

Figure 2


B
A
B
C
hPD-1 1 P P . T F F P A L L V V T E G D N A T F T C S F S N T S E S F V L N W Y R M S P 39
hIgL-κ 1 Q M . T Q S P S S L S A S V G D R V T F T C R S S Q T I G T Y . . L N W Y Q Q K P 38
hTCRα 1 Q V . E Q S P P D L I L Q E G A N S T L R C N F S D S V N N . . L Q W F H Q N P 37
hBTLA 1 Q L Y I K R Q S E H S I L A G D P F E L E C P V K Y C A N R P H V T W C K . . . 38
C'
C"
D
E
hPD-1 40 S N Q T D K L A A F P E D R S Q P G Q D C R F R V T Q L P N G R D F H M S V V R 79
hIgL-κ 39 G . Q A R K L L I F A A S S L L N G V P S R F S G S G S . . G T D F T L T I S S 75
hTCRα 38 W G Q L I N L F Y I P S G T K Q N G . . R L S A T T V A T E R Y S L L Y I S S 74
hBTLA 37 . . . L N G T T C V K L E D R Q T S . . . W K E E K N . . I S F F I L H F E P 67
F
G
hPD-1 80 A R R N D S G T Y L C G A I S L A P . . . K A Q I K E S L R A E L R 110
hIgL-κ 76 L Q P E D F A T Y Y C Q Q S H S A P . . . P Y T F G Q G T R L E M K 106
hTCRα 75 S Q T T D S G V Y F C A A L D L W G G A D G L T F G K G T H L I I Q 105
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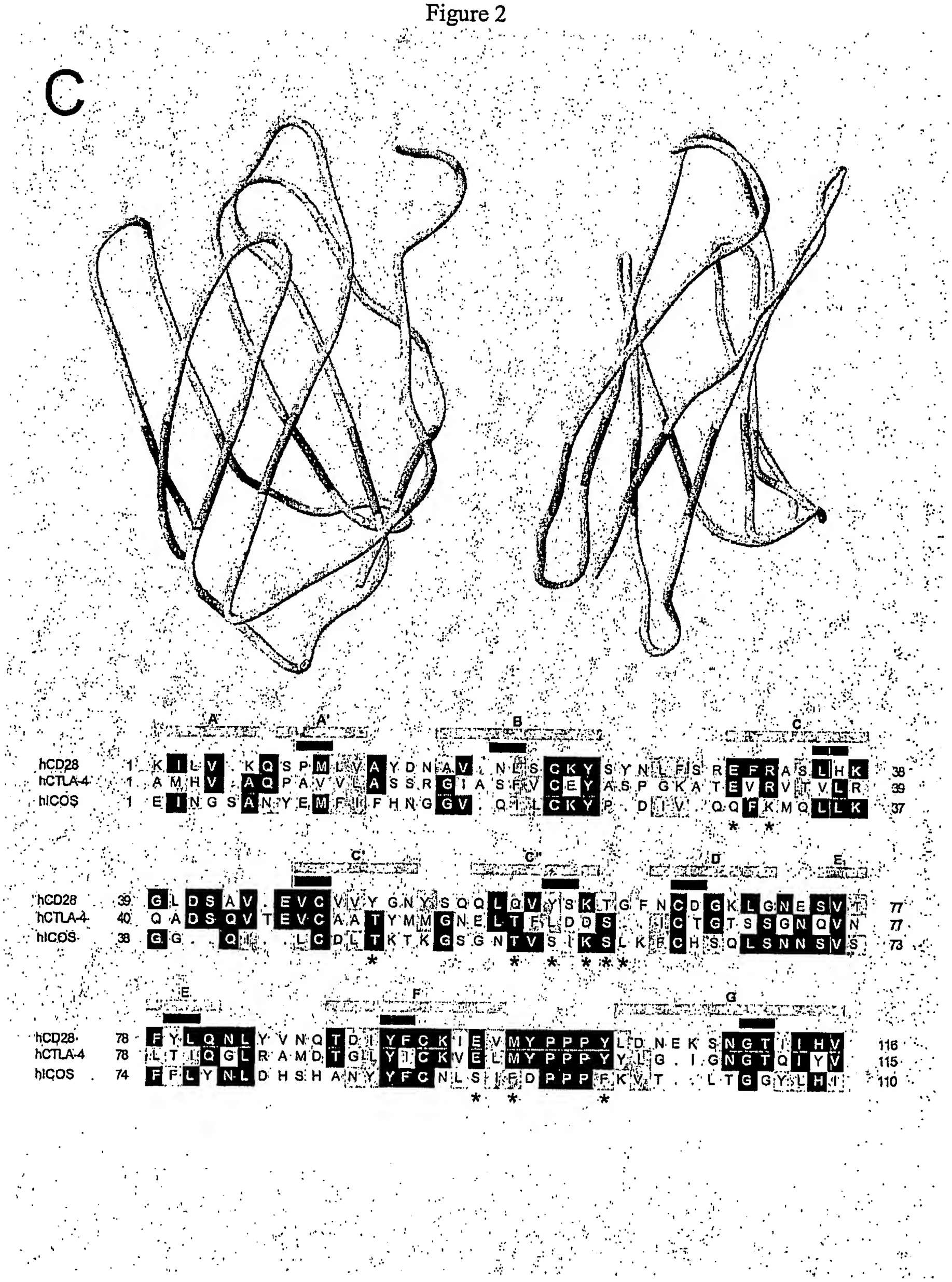
Figure 2


C
A
A'
B
C
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hCTLA-4 1 A M H V A Q P A V V L A S S R G I A S F V C E Y A S P G K A T E V R V T V L R 39
hICOS 1 E I N G S A N Y E M F I F H N G G V Q I L C K Y P D I V Q Q F K M Q L L K 37
C'
C"
D
E
hCD28 39 G L D S A V E V C V V Y G N Y S Q Q L Q V Y S K T G F N C D G K L G N E S V T 77
hCTLA-4 40 Q A D S Q V T E V C A A T Y M M G N E L T F L D D S I C T G T S S G N Q V N 77
hICOS 38 G G Q L L C D L T K T K G S G N T V S I K S L K F C H S Q L S N N S V S 73
E
F
G
hCD28 78 F Y L Q N L Y V N Q T D I Y F C K I E V M Y P P P Y L D N E K S N G T I I H V 116
hCTLA-4 78 L T I Q G L R A M D T G L Y I C K V E L M Y P P P Y Y L G I G N G T Q I Y V 115
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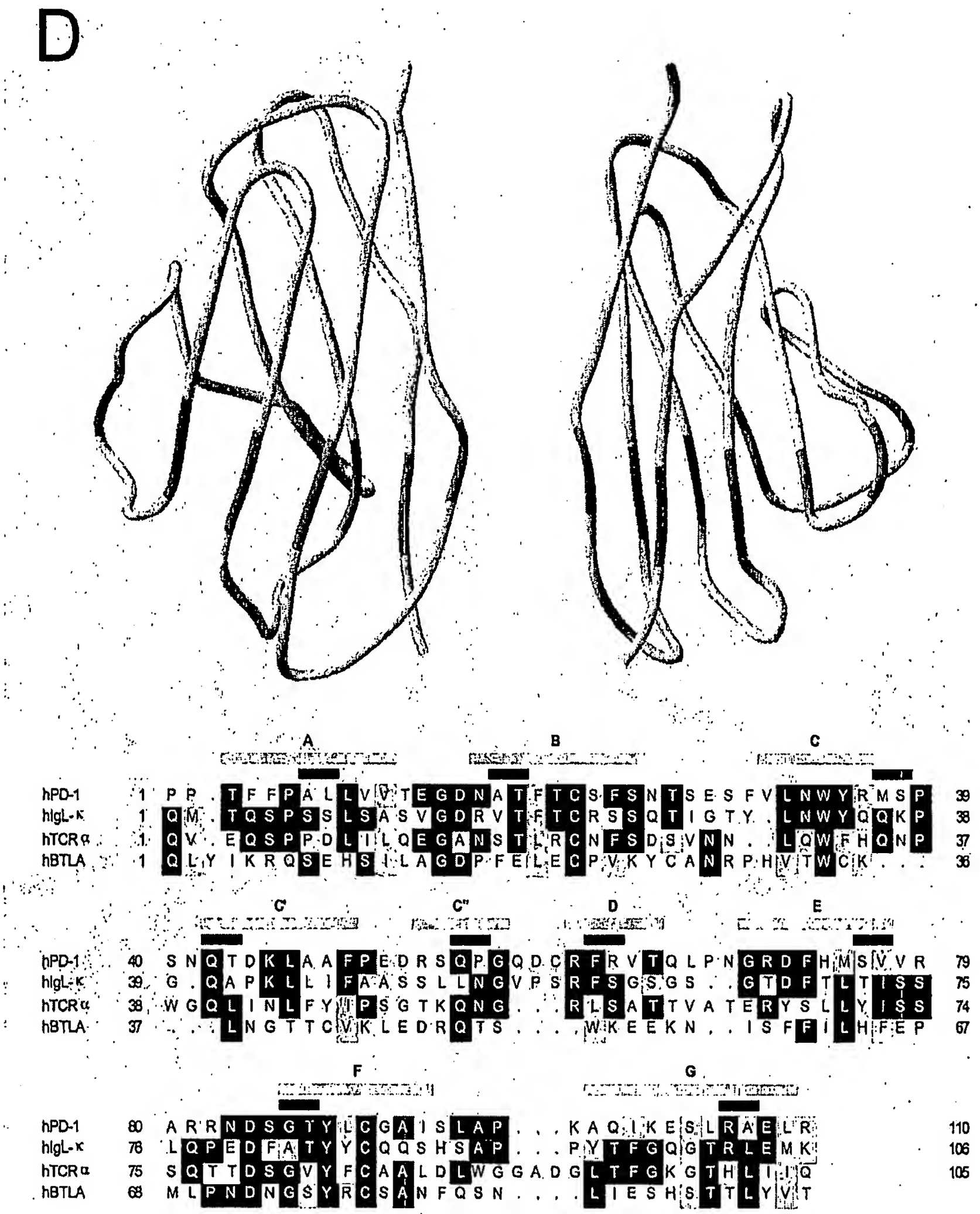
Figure 2


D
A
B
C
C'
C"
D
E
F
G
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hIgL-κ 1 QM.TQSPSSLSASVGDRVTFTCRSSQTIGTY..LNWYQQKP 38
hTCRα 1 QV.EQSPPDLILQEGANSTLRCNFSDSVNN..LQWFHQNP 37
hBTLA 1 QLYIKRQSEHSILAGDPFELECPVKYCANRPHVTWCK... 36
hPD-1 40 SNQTDKLAAFPEDRSQPGQDCRFRVTQLPNGRDFHMSVVR 79
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hTCRα 38 WGQLINLFYIPSGTKQNG...RLSATTVATERYSLLYISS 74
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hPD-1 80 ARRNDSGTYLCGAISLAP...KAQIKESLRAELR 110
hIgL-κ 76 LQPEDFATYYCQQSHSAP...PYTFGQGTRLEMK 106
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